Abstract

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Title of Thesis: Evaluation of potential Alzheimer's disease drugs as prolyloligopeptidase inhibitors

Alzheimer’s disease (AD), which now seems to be one of the most common types of dementia, is alarming health, economic and social threat worldlwide. Despite of significant progression in research during the last decade, casual treatment remains still unknown. Treatment of AD is limited only to suppression of the symptoms by centrally acting inhibitors of acetylcholinesterase and memantine. Enzyme prolyloligopeptidase (POP) plays a role in regulation of neuronal peptides levels and therefore POP has gained attention as one of possible target for the treatment of neuronal disorders. Because effect of POP inhibitors on cognitive functions improvement was reported, the aim of this thesis was to determinate the inhibitory aktivity of newly prepared substabces. These substances were primarily designed as acetylcholinesterase inhibitors with potential N-methyl-D-aspartate (NMDA) receptor antagonism. Additional POP inhibitory potential of novel compounds would even better fit into a concept of multi-target directed ligands (MDTL). Spectrophotometric method with Z-Gly-Pro-p-nitroanilide as the substrate was used to test the inhibitory potential. However, the results showed that the substances had a very low affinity for POP. Based on these *in vitro* data their furhter use as developmental inhibitors can not be expected.